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Hand Grip strength and Cardiovascular Risk Factors in older adult across Europe

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Hand Grip Strength and Cardiovascular Risk Factors in older adult across Europe

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Resumo

A associação entre força de mão (FM) e doença cardiovascular (DCV) tem vindo a ser descrita na literatura, sendo no entanto, ainda mal compreendida. Na tentativa de um melhor entendimento desta associação, têm surgido estudos, embora com resultados contraditórios, que colocam a hipótese dos fatores de risco cardiovasculares (FRCV), além da influência no desenvolvimento de DCV, também serem mediadores na diminuição da FM. Este estudo pretende, por um lado analisar a associação entre a FM e os FRCV e por outro, comparar esta associação em indivíduos com e sem história de DCV prévia (enfarte agudo do miocárdio e acidente vascular cerebral).

Nesta análise vertical, utilizaram-se dados relativos aos participantes da onda 4 de uma base de dados multidisciplinar europeia, (Survey of Health, Ageing, and Retirement in Europe -SHARE) que incluía informação socioeconómica e de saúde.

A FM foi considerada como variável dependente, tendo sido usados como variáveis explanatórias, dados sociodemográficos (idade, sexo, anos de educação) e fatores de risco cardiovasculares (história de DCV prévia, diabetes, excesso de peso ou obesidade, hipertensão, inatividade física, tabagismo) assim como número de doenças crónicas.

De um total de 58 489 indivíduos, selecionaram-se 31 558 indivíduos com idade igual ou superior a 50 anos (idade média = 65.24, dp=9.98 anos, 56% mulheres). Destes, 16,9% dos indivíduos (n = 5318) relataram história de DCV prévia. Devido às diferenças significativas nos valores de FM entre os sexos, a análise subsequente foi realizada estratificada para o sexo. Usando modelos de regressão multinível univariados (não ajustados), foi encontrada uma associação significativa de todas as variáveis explicativas estudadas com FM em indivíduos do sexo masculino e feminino sem história de DCV, com exceção do IMC em indivíduos do sexo feminino. Além disso, em ambos os sexos em indivíduos com história prévia de DCV houve uma associação significativa entre FM e inatividade física, número de doenças crônicas, IMC e anos de escolaridade. Não obstante, foi também encontrada uma associação significativa em indivíduos do sexo feminino com diabetes, hipertensão e tabagismo. Utilizando modelos de regressão multinível multivariada e consequentemente ajustando o efeito de cada variável para as restantes no modelo, foi encontrado o mesmo padrão de associações entre FM e variáveis explicativas, com exceção do IMC em indivíduos do sexo feminino sem história de DCV, que se tornou significativamente associado à FM quando ajustado às demais variáveis.

O nosso estudo demostrou uma associação entre FM e FRCV em indivíduos com e sem CVD, o que sugere que a associação entre FM e CVD possa ser usada como um marcador cumulativo dos FRCV.

Palavras-chave: fatores de risco, doença cardiovascular, envelhecimento, força de mão.

Abstract

The association between hand grip strength (HGS) and cardiovascular disease (CVD) has been described in literature; however, this association is poorly understood, with contradictory results. A possible explanation for this association is the hypothesis of cardiovascular risk factors (CVRF), in addition to their role in the development of CVD, being also mediators in a decrease of hand grip strength. This study aims to evaluate the association between HGS and CVRF and also to compare this association in individuals with and without previous CVD (heart attack and stroke).

In this cross-sectional analysis, we used data from participants aged 50 or older in wave 4 of the Survey of Health, Ageing, and Retirement in Europe (SHARE) database. HGS was considered as a dependent variable, and age, sex, years of education, physical inactivity, body mass index (BMI), diabetes, hypertension, the number of chronic diseases and smoking status were used as explanatory variables. From a total of 58489 individuals, 31558 individuals aged 50 or older (mean age = 65.24, sd=9.98 year old; 56% female) were selected. From this 16.9 % (n=5318) self-reported history of previous CVD. Due to the significant differences in HGS values between sex the subsequent analysis were performed stratified by sex. Using univariable and multivariable multilevel regression models, a significant association of all studied explanatory variables with HGS was found in male and female individuals with no history of CVD; BMI in female individuals, become significantly associated to HGS when adjusted for the other variables. Furthermore, in both gender with a previous history of CVD a significant association was found between HGS and the explanatory variables. The study showed an association between HGS with CVRF in individuals with and without previous CVD, which suggests that HGS could be used as a cumulative marker of CVRF.

Keywords: Risk factors, Cardiovascular disease, Ageing, Grip strength.

Introduction

The number of people worldwide aged over 60 years is expected to be more than double by 2050 and more than triple by 2100 [1]. This increased life expectancy is associated with higher prevalence of non-communicable chronic diseases, morbidity and disability [2].

Globally, cardiovascular diseases (CVD), which include coronary heart disease, stroke, rheumatic heart disease, cardiomyopathy, and other heart diseases, represent the leading worldwide cause of death in developing countries [3].

There are several studies showing an association between frailty, a clinical syndrome, characterized by physical weakness and decreased physiologic reserve, and prevalent CVD in the community [4]. Moreover, subclinical CVD had also been described as an important contributor to frailty [5]. Mechanisms of frailty biology involve up-regulation of inflammatory cytokines, and a dysregulation of the immune, hormonal, and endocrine systems [6,7]. This chain of metabolic processes is also highly linked to a progressive decline in muscle mass and strength, when breakdown exceeds muscle building. Indeed, age-related decline in muscle functioning may result from the presence of chronic, low-level inflammation, as poor muscle strength [8]. The same mechanisms at the level of immune cells and pro-inflammatory cytokines involved in atherosclerosis development in the arterial wall are thought to be responsible for cell senescence, changing body composition to promote frailty. [6]

Frailty may predispose, and is apparently related, to many CVD such as heart failure. Grip strength (GS) measurement has been recommended by the European Working Group on Sarcopenia in Older People (EWGSOP) to assess muscle strength. Indeed, HGS when compared with others muscular tests such as the trunk and knee extension or flexion, is considered the most appropriate marker of muscle strength [9]. Moreover, it is an easy and cheap test to be carried out by trained individuals without clinical practice. HGS is a standard tool to measure and evaluate sarcopenia and it is one of the measures used in Fried Frailty Scale [6]. Low HGS values have been associated with disability, frailty, lower health-related quality of life and higher mortality, including cardiovascular-related mortality [10]. Indeed, reduced HGS was found to be a predictor of cardiovascular (CV) mortality, as well as systolic blood pressure, and a better predictor of all causes of mortality [10].

However, the association between HGS and CVD is still under debate. Other studies shows that lower HGS is associated with increased susceptibility to CV death [6][10], a recent study demonstrated that, when CV absolute risk was taken into account, HGS was not found to be predictive of incident CV events [11]. The association between muscle strength, measured by HGS, and some cardiovascular risk factors (CVRF), including metabolic markers had been previously evaluated. The authors related only a moderate association between HGS and CV risk markers, which led them to conclude that the effect of muscle strength on CVD does not seem to be mediated by CVRF [12].

Considering the lack of evidence, this study aims to assess the association between HGS and CVRF namely, age, diabetes, body mass index (BMI), hypertension, smoking status, physical inactivity and number of chronic diseases, taking into account gender and years of education, in a large European senior's database. Additionally, we also aimed to compare this association between two subgroups, individuals with and without previous history of CVD (heart attack and stroke).

Material and methods

Data collection

This paper uses data from SHARE Wave 4 release 1.1.1, as of March 28th 2013 (DOI: 10.6103/SHARE.w4.111). SHARE (Survey of Health, Ageing, and Retirement in Europe) project is an European cross-national panel database, which includes detailed questions on demographics, health, social and economic status from representative samples of the community-based population. We used data from wave 4, which includes data collected in Austria, Germany, Sweden, Netherlands, Spain, Italy, France, Denmark, Switzerland, Belgium, Czech Republic, Poland, Ireland, Hungary, Slovenia, Estonia and Portugal [13] [14]. Designed on the basis of the US Health and Retirement Study and the English Longitudinal Study of Ageing, SHARE contains data from a very large population; with a harmonized cross-national design which allows consistent international comparisons, with a large number of dimensions simultaneously, providing a dynamic picture of ageing in Europe. A detailed description of the SHARE data and methodology has been published and is available to registered users on the SHARE website (http://www.share-project.org).

It is a cross-sectional analysis study which wave contains data from 58,489 individuals between the ages of 23 and 103 (in 2010). For the purpose of the present study, the sample includes non-institutionalized individuals with 50 years old or more, with a BMI higher than 18.5 kg/m2, and who answered all of the questions included in this analysis (dependent and independent variables). We excluded data from three countries (Germany, Poland and Sweden) due to the low number of individuals included in this wave who met the inclusion criteria and after exclusion of cases with missing values (less than 5%).

Dependent variables – HGS measure

A hand dynamometer was used to access HGS, which was measured in both hands or in one hand twice, and their maximum value defines the variable *max grip.* Valid measurements were defined as the values of two measurements in one hand that differed by less than 20 kg and were included between 0 and 100kg. Despite detailed information to the participants about the position and the performing of the test, and instructed to verbally motivate the respondents to squeeze the hands as hard as possible; a protocol was used by the interviewers for evenly measured of the HGS. This information generated a continuous variable.

Explanatory variables

Due to the large and extent information of the SHARE database we were able to include a huge diversity of putative explanatory variables in our study.

Socio-demographic variables were included in our study, such as age, gender and years of education.

Age was calculated as the difference between the year 2010 and the date of birth, and four age classes were set (50-54, 55-64, 65-74 and more than 75 years old). The gender response generated a dichotomous variable, male or female. The education years variable, resulted from the response to the question “years of education”, which was dichotomized as ≤ 12 years or as > 12 years of education.

We also included CVRF, the namely self-reported presence or absence of previous CVD (heart attack and stroke), high blood pressure or hypertension, diabetes or high blood sugar, smoking status, BMI, physical inactivity, as well as the number of chronic diseases.

History of vascular diseases were dichotomized according to self-reported presence or absence of physician-diagnosed vascular diseases: “Has a doctor ever told you that you had/Do you currently have any of the conditions...”; “A heart attack including myocardial infarction or coronary thrombosis or any other heart problem including congestive heart failure”; “High blood pressure or hypertension”; “A stroke or cerebral vascular disease”; “Diabetes or high blood sugar”.

Smoking status (current smoker or former) was also included as CVRF, being dichotomized as never smoked and smoker or history of smoking. The continuous variable BMI was transformed into a discrete variable with three classes (18.5-24.9, 25-29.9 and more than 30 kg/m2). Individuals with BMI lower than 18.5 were excluded from the study due to the small number in the sample and the association of low BMI with malnutrition, weak states or even cachexia.

The variable “number of chronic diseases” was based on the number of chronic diseases reported by each individual, which was dichotomized by ≤ 2 or >2 chronic diseases.

Physical inactivity was assessed on the basis of the following questions: “How often do you engage in activities that require a moderate level of energy such as gardening, cleaning the car, or doing a walk?” and “We would like to know about the type and amount of physical activity you do in your daily life. How often do you engage in a vigorous physical activity, such as sports, heavy housework, or a job that involves physical labor?”. These questions addressed the levels of vigorous and moderate physical activity, respectively. Physical inactivity was defined as never, or almost never, engaging in moderate or vigorous physical activity.

Statistical analysis

Given the multilevel structure of data, with individuals nested in each country, a multilevel regression approach was used, considering the HGS as the dependent variable.

In a first approach, univariable multilevel regression models were performed, considering each covariate, to identify potential factors associated with the outcome variable.

Then, all variables were analyzed in the multivariable multilevel regression model. The final model included only the statistical significant covariates, based on a backward selection method. Regression coefficients and 95% confidence intervals (CI) are reported. The significance level was set at 0.05. All analyses were performed using the software IBM SPSS (version 23).

Results

From the total of 58 489 participants in wave 4 of the SHARE survey, 53 218 showed HGS values between 0Kg and 100Kg. From this sample, 372 (0.7%) individuals were excluded as they showed a BMI lower than 18.5 kg/m^2. Furthermore, 34.7% (n=18.482) was excluded due to the missing value of BMI, 1.3% (n=717) due to implausible answers, 1.2% (n=628) due to "don´t know" response and 0.3% (n=168) due to refusal of BMI response. Also individuals with missing codes ("refusal" and "don´t know") and those who had not answer in any of the other variables. From the 31676 individuals that remained, due to significantly low values in geographical distribution (Annexed table 1), Germany (0.1%), Poland (0.1%) and Sweden (0.2%) were also excluded, leading to a final sample of 31558 individual (Figure 1). From these, 56% are females (17 677 females) 44% are males (13 881 males) with a mean age of 65.24 (SD= 9.98) years old. The mean age for male was 65.18 (SD=10.05) years old. Globally, HGS mean was 43.70Kg (SD= 10.52) in males and 27.02Kg (SD=7.25) in females ($p<0.001$). Due to the significant differences in HGS values between sex the subsequent analysis were performed stratified by sex.

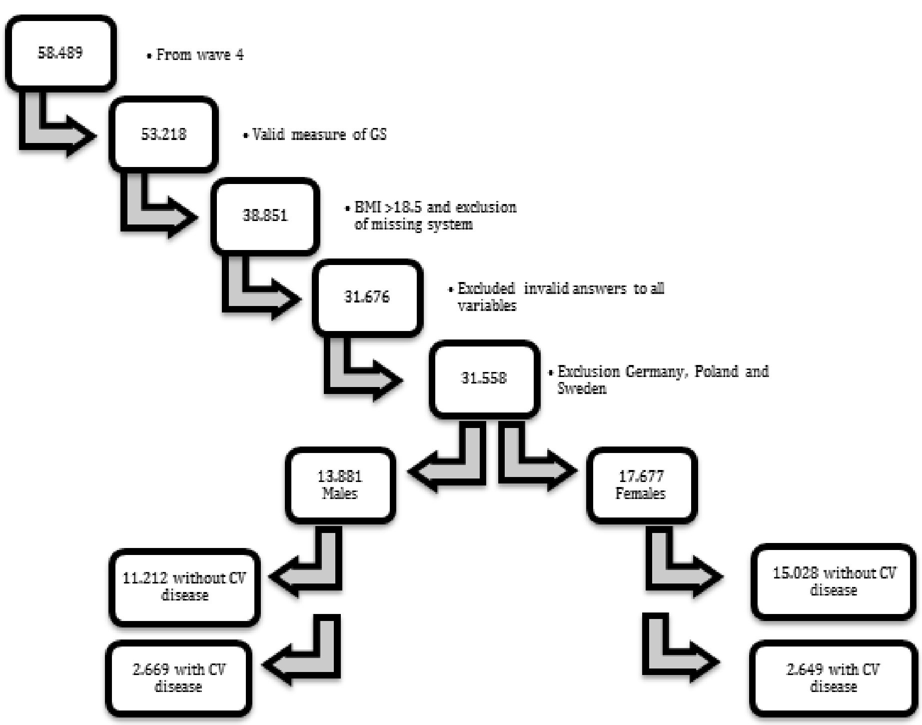

Figure 1. Diagram of selection of the final sample.

From the 31558 individuals, 16.9% (n=5318) self-reported history of previous CVD. From these we found 50.2% (n=2 669) males and 49.8% (n=2 649) females. Among the 83.1% (n=26 240) who did not report CVD, 42.7% (n=11 212) were males and 57.3% (n=15 028) females.

Using univariable multilevel regression models, we found a significant association between HGS and all studied explanatory variables, in males and females without a history of CVD, with exception of BMI in female individuals. Furthermore, in both gender with previous history of CVD, a significant association was found between HGS and physical inactivity, a number of chronic diseases, BMI and years of education. Moreover, in females we also found a significant association between HGS and diabetes, hypertension and smoking (tables 1 and 2). Results of the multilevel multivariable regression models revealed the same associations between HGS and the explanatory variables, with exception of BMI in female individuals with no history of CVD, which become significantly associated with HGS when adjusting for the remaining significant variables (tables 1 and 2). Considering the subset of individuals without previous CVD, it was found that increase in ageing, lower number of years of education, physical inactivity, more than 2 chronic diseases, overweight or obesity, smoking, hypertension and diabetes were significant predictors of lower HGS. A similar pattern of association with HGS was seen in other groups. However, in the males with previous history of CVD (Heart attack and/or stroke) the explanatory variables diabetes/high blood sugar, hypertension/high blood pressure, smoke and age, lost their statistical significance after adjusting for the remaining variables in the model.

Table 1. Association of explanatory variables with HGS (univariable and multivariable models) in female individuals stratified according to previous history or no history of CVD.

	No history of CVD (no heart attack neither stroke)								Previous history of CVD (Heart attack and/or stroke)							
	Unadjusted				Adjusted				Unadjusted				Adjusted			
	b	p	IC95%		b	p	IC95%		b	p	IC95%		b	p	IC95%	
Constant	-	-	-	-	29.45	<0.001	28.49	30.41	-	-	-	-	26.42	<0.001	25.44	27.39
Physical inactivity (yes)	-4.71	<0.001	-5.10	-4.32	-4.04	<0.001	-4.42	-3.67	-4.95	<0.001	-5.61	-4.29	-4.35	<0.001	-5.00	-3.71
Number chronic diseases (>2)	-3.67	<0.001	-3.94	-3.99	-2.96	<0.001	-3.26	-2.66	-2.75	<0.001	-3.40	-2.11	-1.78	<0.001	-2.49	-1.07
BMI *																
BMI (25-29.9)	0.16	0.226	-0.10	0.41	0.72	<0.001	0.48	0.96	0.56	0.007	-0.14	1.26	0.88	0.009	0.215	1.54
BMI (≥30)	0.07	0.649	-0.23	0.36	1.41	<0.001	1.12	1.71	1.00	<0.001	0.27	1.73	1.84	<0.001	1.13	2.54
Education (>12-y)	1.89	<0.001	1.64	2.14	1.52	<0.001	1.28	1.76	3.31	<0.001	2.56	4.05	2.64	<0.001	1.93	3.34
Diabetes or high blood sugar (yes)	-2.58	<0.001	-2.96	-2.21	-0.77	<0.001	-1.16	-0.38	-1.56	<0.001	-2.23	-0.88	-0.74	0.029	-1.40	-0.08
High blood pressure or hypertension (yes)	-1.77	<0.001	-2.00	-1.54	-0.60	<0.001	-0.85	-0.36	-1.80	<0.001	-2.40	-1.19	-0.763	0.021	-1.41	-0.12
Smoke (yes)	-1.53	<0.001	-1.77	-1.30	-1.40	<0.001	-1.62	-1.18	-2.48	<0.001	-3.11	-1.85	-2.05	<0.001	-2.65	-1.46
Age, years *																
Age (55-64)	-0.56	0.001	-0.89	-0.22	-0.52	0.001	-0.84	-0.20	-0.05	0.911	-0.91	0.81	-	-	-	-
Age (65-74)	-0.85	<0.001	-1.19	-0.50	-0.71	<0.001	-1.042	-0.378	0.02	0.961	-0.88	0.93	-	-	-	-
Age (>75)	-1.25	<0.001	-1.63	-0.87	-1.07	<0.001	-1.43	-0.71	-0.68	0.165	-1.63	0.28	-	-	-	-

*Reference classes for BMI is 18.5-24.9 Kg/m2 and for age is 50-54 years old.

Table 2. Association of explanatory variables with HGS (univariable and multivariable models) in male individuals stratified according to previous history or no history of CVD.

	No history of CVD (no heart attack neither stroke)								Previous history of CVD (Heart attack and/or stroke)							
	Unadjusted				Adjusted				Unadjusted				Adjusted			
	b	p	IC95%		b	p	IC95%		b	p	IC95%		b	p	IC95%	
Constant	-	-	-	-	44.67	<0.001	42.92	46.43	-	-	-	-	39.32	<0.001	37.61	41.03
Physical inactivity (yes)	-6,97	<0.001	-7.74	-6.21	-6.44	<0.001	-7.19	-5.70	-7.84	<0.001	-8.84	-6.84	-7.55	<0.001	-8.53	-6.57
Number chronic diseases (>2)	-3.90	<0.001	-4.41	-3.40	-2.87	<0.001	-3.42	-2.31	-1.92	<0.001	-2.74	-1.10	-1.75	<0.001	-2.53	-0.97
BMI *																
BMI (25-29.9)	2.77	<0.001	2.34	3.19	3.04	<0.001	2.63	3.46	3.02	<0.001	2.08	3.96	2.92	<0.001	2.03	3.82
BMI (≥30)	3.47	<0.001	2.95	4.00	4.68	<0.001	4.16	5.21	5.05	<0.001	4.01	6.09	5.42	<0.001	4.42	6.42
Education (>12-y)	1.48	<0.001	1.07	1.90	1.47	<0.001	1.07	1.87	1.71	<0.001	0.78	2.62	1.51	0.001	0.65	2.37
Diabetes or high blood sugar (yes)	-3.02	<0.001	-3.60	-2.43	-2.23	<0.001	-2.84	-1.63	-0.71	0.154	-1.68	0.27	-	-	-	-
High blood pressure or hypertension (yes)	-1.35	0.001	-1.74	-0.95	-1.06	<0.001	-1.47	-0.65	-8.38	0.347	-1.18	0.42	-	-	-	-
Smoke (yes)	-0.64	0.002	-1.03	-0.26	-0.85	<0.001	-1.22	-0.48	-0.64	0.131	-1.48	0.19	-	-	-	-
Age, years *																
Age (55-64)	-0.90	<0.001	-1.47	-0.33	-0.86	0.002	-2.11	-0.88	0.79	0.205	-0.43	2.02	-	-	-	-
Age (65-74)	-1.50	<0.001	-2.09	-0.91	-1.36	<0.001	-1.93	-0.79	0.91	0.161	-0.36	2.18	-	-	-	-
Age (>75)	-1.57	<0.001	-2.21	-0.93	-1.50	<0.001	-1.40	-0.31	0.66	0.342	-0.70	2.01	-	-	-	-

*Reference classes for BMI is 18.5-24.9 Kg/m2 and for age is 50-54 years old.

Discussion

An association between HGS and CVD has been described in other studies [6,10]. Although several possible reasons for this association include CVRF, this is not yet well understood. Some authors advocate that low HGS on CV events might be partly mediated by CVRF; however, using a large panel of CVRF, focalized on biochemical parameters, this association could not be established, in previous studies[12]. In the present study, using data from wave 4 of SHARE database, we assessed the association between HGS and traditional CVRF (the explanatory variables) also including socio-demographic variables as gender and years of education. Additionally, we also evaluated this association in individuals with and without known previous CVD (heart attack and stroke). The results in the present showed an association between HGS and most of the studied CVRF, suggesting that HGS could be used as a cumulative marker of CVRF.

HGS has been widely used as a tool to assess frailty and sarcopenia in the CV community. In fact, it has become a reliable measure to identify the low functional state in CV patients [6]. It is yet uncertain if HGS can be a consequence of subclinical CVD or premature finding in a relatively low-risk population before established CVD. As frail patients tend to exhibit deterioration before they manifest clinical CVD [6], the same CVRF were studied in individuals with and without CVD.

In this study the results showed that, considering the subset of individuals without previous CVD, all studied explanatory variables were associated with HGS for both sexes. Indeed, lower HGS was found to be associated with increasing ageing, lower number of years of education, physical inactivity, more than 2 chronic diseases, overweight or obesity, smoking, hypertension and diabetes. However, considering the subset of individuals with previous established CVD, age was not associated with HGS for both sex. However, in this group, we found differences between both sex; the variables being smoker, the presence of hypertension and diabetes were not associated with HGS in males. The associations between HGS and the variables included in this work have already been established in literature in individuals without history of CVD [4, 15, 16]. Nevertheless, there is a lack of information about these associations in individuals with previous history of CVD.

Common to all studied groups, are a higher level of education, and therefore high socio-cultural background, is associated with better preventive measures of health, changes in lifestyle and adhesion to treatments. The addiction of numerous chronic diseases contributes to morbidity, which can be reflected by a decrease in HGS and, depending on its etiology, may exacerbate the CV condition[17]. According to literature, muscle strength and CV events may be explained by endothelial dysfunction, arterial stiffness and autonomic imbalance which can be prevented or improved by physical activity [18] [19]. BMI higher than 25 kg/m^2 is described as a CVRF and seems to be associated with HGS; however, paradoxically, overweight or obesity is associated with higher HGS. Indeed, BMI does not reflect body composition [20], so despite muscle mass may be decline by around 25% between the ages of 50 and 75 years [21], high BMI may reflect not just a higher fat index, but also a higher muscle mass [22]. On the other hand, men are reported to have a significantly higher percentage of visceral adiposity [23], which can have less impact in the performance of HGS.

Also, not surprisingly, low-level inflammation and poor nutritional status following ageing, may show a decrease in HGS [5] [8]; however, this study showed that age is not associated with HGS in individuals with a history of CVD. This finding may suggest that CVD, leading to decreased organ system functions, related with low CV fitness involved in decrease of HGS, can have a higher impact on the patients prognosis than age, that may count as a minor independent factor, reflecting the heterogeneity of the aging process.

Moreover, among individuals with previous established CVD, diabetes, hypertension and smoking was only associated with HGS in females. Hormonal responses may play a role related to decreasing of estrogen production in postmenopausal women, leading to increased central fat accumulation, reduction in lean body mass, which may mediate muscle impairment [11].

This study brings a valuable contribution since it included a large cohort of cross-national European aged more than 50, following a standardized protocol, harmonized with other aging studies, which allows generalization of the findings. However, some limitations of this study require discussion. Firstly, the impacts of other CVRF on HGS were not evaluated and due to cross-sectional study design, the causal relationship between muscle strength and CVRF should be better clarified, taking account repeated measures along time. Additionally, SHARE study only included non-institutionalized participants, and it is well known that people who volunteer to participate in research surveys like SHARE are likely to be more motivated and healthier. As a result, a high proportion of older people with multiple chronic conditions might have been excluded. Moreover, some variables presented high non-response ratios, which might affect the results. Health data are self-reported which is criticized by some authors and considered reliable according to others. Moreover, this is a cross-sectional data analysis that precludes the assessment of any causal effect of HGS on CVRF. Finally we did not measure the quantity of muscle mass, so the effect of muscle quantity on the muscle strength may be overlooked.

In conclusion, this study showed an association between HGS with CVRF in individuals with and without previous CVD. These results highlight the importance of HGS measurement, which could be identify in the clinical setting, along with other CVRF, patients at higher risk of a CV event. Since most CV events occur in individuals without known CVD, in subsets with particular characteristics such as women and diabetics, the earlier evaluation, including HGS assessment, could improve clinical insight about unknown disturbances in multiple organ systems. Thus, the result of this study suggests that, HGS could be used as a cumulative marker of CVRF.

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Supplementary material Table 1 – Descriptive of population

	Austria	Germany	Sweden	Netherlands	Spain	Italy	France	Denmark	Switzerland	Belgium	Czechia	Poland	Hungary	Portugal	Slovenia	Estonia
Selected cases, %	3585 (11.3%)	16 (0.1%)	65 (0.2%)	737 (2.3%)	1204 (3.9%)	1195 (3.8%)	3144 (9.9%)	427 (1.3%)	2316 (7.3%)	2593 (8.2%)	4091 (12.9%)	37 (0.1%)	2714 (8.6%)	1493 (4.7%)	2305 (7.3%)	5718 (18.1%)
Gender, women (%)	2015 (56.2%)	11 (68.8%)	35 (53.8%)	402 (54.5%)	648 (52.3%)	633 (53.0%)	1738 (55.3%)	218 (51.1%)	1212 (52.3%)	1385 (53.4%)	2314 (56.6%)	21 (56.8%)	1540 (56.7%)	835 (55.9%)	1283 (55.7%)	3454 (60.4%)
Age, years																
>75	471 (13.1%)	2 (12.5%)	13 (20.0%)	128 (17.4%)	265 (21.4%)	168 (14.1%)	601 (19.1%)	104 (24.4%)	499 (21.5%)	568 (21.9%)	1025 (25.1%)	9 (24.3%)	478 (17.6%)	353 (23.6%)	505 (21.9%)	1067 (18.7%)
65-74	1091 (30.4%)	1 (6.3%)	24 (36.9%)	213 (28.9%)	289 (23.3%)	336 (28.1%)	885 (28.1%)	100 (23.4%)	666 (28.8%)	941 (36.3%)	1139 (27.8%)	13 (35.1%)	727 (26.8%)	426 (28.5%)	715 (31.0%)	1510 (26.4%)
55-64	1348 (37.6%)	10 (62.5%)	20 (30.8%)	263 (35.7%)	427 (34.4%)	502 (42.0%)	1150 (36.6%)	161 (37.5%)	839 (36.3%)	938 (36.2%)	1378 (33.7%)	11 (29.7%)	1216 (44.8%)	490 (32.8%)	765 (33.2%)	1964 (34.3%)
50-54	675 (18.8%)	3 (18.8%)	8 (12.3%)	133 (18.0%)	259 (21.9%)	189 (15.8%)	508 (16.2%)	62 (14.5%)	312 (13.5%)	146 (5.8%)	549 (13.4%)	4 (10.8%)	293 (10.8%)	224 (15.0%)	320 (13.9%)	1177 (20.6%)
Education, years																
>12-y	700 (19.5%)	5 (31.3%)	22 (33.8%)	326 (44.2%)	254 (20.5%)	322 (26.9%)	956 (30.4%)	316 (74.0%)	407 (17.6%)	1170 (45.1%)	1628 (39.8%)	5 (13.5%)	433 (16.0%)	152 (10.2%)	466 (20.2%)	2033 (35.6%)
≤12-y	2885 (80.5%)	11 (68.8%)	43 (66.2%)	411 (55.8%)	986 (79.5%)	873 (73.1%)	2188 (69.6%)	111 (26.0%)	1909 (82.4%)	1423 (54.9%)	2463 (60.2%)	32 (86.5%)	2281 (84.0%)	1341 (89.8%)	1839 (79.8%)	3685 (64.6%)
BMI																

	Austria	Germany	Sweden	Netherlands	Spain	Italy	France	Denmark	Switzerland	Belgium	Czechia	Poland	Hungary	Portugal	Slovenia	Estonia
	713 (19.9%)	0 (0.0%)	12 (18.5%)	113 (15.3%)	269 (21.7%)	196 (16.4%)	611 (19.4%)	75 (17.6%)	316 (13.6%)	519 (20.0%)	1099 (26.9%)	6 (16.2%)	823 (30.3%)	338 (22.6%)	569 (24.7%)	1665 (29.1%)
25-29.9	1474 (41.1%)	8 (50.0%)	28 (43.1%)	319 (43.3%)	555 (44.8%)	516 (43.2%)	1223 (38.9%)	164 (38.4%)	881 (38.0%)	995 (38.4%)	1794 (43.9%)	14 (37.8%)	1093 (40.3%)	648 (43.4%)	1051 (45.6%)	2258 (39.5%)
18.5-24.9	1398 (39.0%)	8 (50.0%)	25 (38.5%)	305 (41.4%)	416 (33.5%)	483 (40.4%)	1310 (41.7%)	188 (44.0%)	1119 (48.3%)	1079 (41.6%)	1198 (29.3%)	17 (45.9%)	798 (29.4%)	507 (34.0%)	685 (29.7%)	1795 (31.4%)
Smoking																
Smoker	2024 (56.5%)	10 (62.5%)	46 (70.8%)	315 (42.7%)	685 (55.2%)	633 (53.0%)	1611 (51.2%)	203 (47.5%)	1161 (50.1%)	1246 (48.1%)	2251 (55.0%)	19 (51.4%)	1403 (51.7%)	993 (66.5%)	1404 (60.9%)	3161 (55.3%)
No	1561 (43.5%)	6 (37.5%)	19 (29.2%)	422 (57.3%)	555 (44.8%)	562 (47.0%)	1533 (48.8%)	224 (52.5%)	1155 (49.9%)	1347 (51.9%)	1840 (45.0%)	18 (48.6%)	1311 (48.3%)	500 (33.5%)	901 (39.1%)	2557 (44.7%)
Physical inactivity																
No	250 (7.0%)	0 (0.0%)	3 (4.6%)	39 (5.3%)	186 (15.0%)	143 (12.0%)	248 (7.9%)	11 (2.6%)	146 (6.3%)	225 (8.7%)	364 (8.9%)	6 (16.2%)	325 (12.0%)	305 (20.4%)	184 (8.0%)	620 (10.8%)
Yes	3335 (93.0%)	16 (100.0%)	62 (95.4%)	698 (94.7%)	1054 (85.0%)	1052 (88.0%)	2896 (92.1%)	416 (97.4%)	2170 (93.7%)	2368 (91.3%)	3727 (91.1%)	31 (83.8%)	2389 (88.0%)	1188 (79.6%)	2121 (92.0%)	5098 (89.2%)
Number of chronic diseases																
>2	874 (24.4%)	4 (25.0%)	14 (21.5%)	139 (18.9%)	345 (27.8%)	227 (19.0%)	698 (22.2%)	52 (12.2%)	350 (15.1%)	724 (27.9%)	1127 (27.5%)	4 (10.8%)	971 (35.8%)	466 (31.2%)	521 (22.6%)	1947 (34.1%)
≤2	2711 (75.6%)	12 (75.0%)	51 (78.5%)	598 (81.1%)	895 (72.2%)	968 (81.0%)	2446 (77.4%)	375 (87.8%)	1966 (84.9%)	1869 (72.1%)	2964 (72.5%)	33 (89.2%)	1743 (64.2%)	1027 (68.8%)	1784 (77.4%)	3771 (65.9%)

	Austria	**Germany**	**Sweden**	**Netherlands**	**Spain**	**Italy**	**France**	**Denmark**	**Switzerland**	**Belgium**	**Czechia**	**Poland**	**Hungary**	**Portugal**	**Slovenia**	**Estonia**
Heart attack																
Yes	373 (10.4%)	1 (6.3%)	10 (15.5%)	74 (10.0%)	144 (11.6%)	99 (8.3%)	370 (11.8%)	22 (5.2%)	172 (7.4%)	288 (11.1%)	581 (14.2%)	3 (8.1%)	552 (21.3%)	161 (10.8%)	310 (13.4%)	1296 (22.7%)
No	3212 (88.5%)	15 (93.8%)	55 (84.6%)	663 (90.0%)	1096 (88.4%)	1096 (91.7%)	2774 (88.2%)	405 (94.8%)	2144 (92.6%)	2305 (88.9%)	3510 (85.8%)	34 (91.9%)	2162 (79.7%)	1332 (89.2%)	1995 (86.6%)	4422 (77.3%)
Stroke																
Yes	159 (4.4%)	0 (0.0%)	3 (4.6%)	20 (2.7%)	28 (2.3%)	21 (1.8%)	87 (2.8%)	12 (2.8%)	56 (2.4%)	83 (3.2%)	179 (4.4%)	1 (2.7%)	173 (6.4%)	66 (4.4%)	77 (3.3%)	388 (6.8%)
No	3426 (95.6%)	16 (100.0%)	62 (95.4%)	717 (97.3%)	1212 (97.7%)	1174 (98.2%)	3057 (97.2%)	415 (97.2%)	2260 (97.6%)	2510 (96.8%)	3912 (95.6%)	36 (97.3%)	2541 (93.6%)	1427 (95.6%)	2228 (96.7%)	5330 (93.2%)
Diabetes or high blood sugar																
Yes	367 (10.2%)	2 (12.5%)	7 (10.8%)	65 (8.8%)	189 (15.2%)	131 (11.0%)	330 (10.5%)	19 (4.4%)	142 (6.1%)	264 (10.2%)	675 (16.5%)	3 (8.1%)	439 (16.2%)	269 (18.0%)	252 (10.9%)	695 (12.2%)
No	3218 (89.8%)	14 (87.5%)	58 (89.2%)	672 (91.2%)	1051 (84.8%)	1064 (89.0%)	2814 (89.5%)	408 (95.6%)	2174 (93.9%)	2329 (89.8%)	3416 (83.5%)	39 (91.9%)	2275 (83.8%)	1224 (82.0%)	2053 (89.1%)	5023 (87.8%)
High blood pressure																
Yes	1296 (36.2%)	6 (37.5%)	30 (46.2%)	192 (26.1%)	461 (37.2%)	394 (33.0%)	964 (30.7%)	90 (21.1%)	651 (28.1%)	839 (32.4%)	1904 (46.5%)	10 (27.0%)	1453 (53.5%)	618 (41.4%)	953 (41.3%)	2766 (48.4%)
No	2289 (63.8%)	10 (62.5%)	35 (53.8%)	545 (73.9%)	779 (62.8%)	801 (67.0%)	2180 (69.3%)	337 (78.9%)	1665 (71.9%)	1754 (67.7%)	2187 (53.5%)	27 (73.0%)	1261 (46.5%)	875 (58.6%)	1352 (58.7%)	2952 (51.6%)

	Austria	Germany	Sweden	Netherlands	Spain	Italy	France	Denmark	Switzerland	Belgium	Czechia	Poland	Hungary	Portugal	Slovenia	Estonia
Total	11.3%	0.1%	0.2%	2.3%	3.9%	3.8%	9.9%	1.3%	7.3%	8.2%	12.9%	0.1%	8.6%	4.7%	7.3%	18.1%